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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/565,573	02/26/2007	Daniel J. Smith	089498.0480.US	2362

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EXAMINER	
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ART UNIT	PAPER NUMBER
1734	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/565,573	SMITH, DANIEL J.	
	Examiner	Art Unit	
	BRITTANY M. MARTINEZ	1734	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 November 2010*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3,4,6-9 and 11-25* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1, 3, 4, 6-9 and 11-25* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of Application

Acknowledgment is made of Applicant's arguments/remarks and amendments filed November 23, 2010. **Claims 1, 3, 4, 6-9 and 11-25** are pending in the instant application, with **Claims 1, 4, 11, 18 and 22** amended. **Claims 2, 5 and 10** have been cancelled. **Claims 1, 3, 4, 6-9 and 11-25** have been examined.

Claim Rejections - 35 USC § 112

1. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2. **Claims 1, 3, 4, 6 and 18-25** are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the original specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The addition of "a combination...and a salt" to amended **Claims 1 and 4** and the addition of "a salt" to amended **Claims 18 and 22** is not supported by the original disclosure. The only support for a salt used to produce nitric oxide in the original disclosure is a salt mixed with a cream, gel, or combination thereof to produce nitric oxide. **Claims 3 and 6** depend from **Claim 1**; **Claims 19-21** depend from **Claim 18**; and **Claims 23-25** depend from **Claim 22**.

Claim Rejections - 35 USC § 102

3. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

4. **Claim 4** is rejected under 35 U.S.C. 102(b) as anticipated by Abrams (US 2,844,546) (of record).

5. With regard to **Claim 4**, Abrams discloses combining a cationic exchange resin having a hydrogen-atom counter ion with a salt (Abrams, col. 7, lines 35-75; col. 8, lines 1-19, in particular). Abrams does not explicitly disclose the combination of the resin and salt producing nitric oxide; however, the combination of the cationic exchange resin having a hydrogen-atom counter ion with a salt would inherently produce nitric oxide. For a reference which neither expressly describes or teaches the subject matter alleged to be anticipated, the reference must provide enough information to permit an inference that the subject matter is inherent. *Ex parte Garvin*, 62 USPQ 2d 1680 (BPAI 2001). Abrams discloses combining a cationic exchange resin having a hydrogen-atom counter ion with a salt (Abrams, col. 7, lines 35-75; col. 8, lines 1-19, in particular), substantially as in the instant application. Thus, the combination of cationic exchange resin with a salt of Abrams would produce nitric oxide to no less an extent than that of the instant

application. Accordingly, the burden shifts to Applicant to show that nitric oxide production would not occur in the process of Abrams.

6. **Claims 1 and 3** are rejected under 35 U.S.C. 102(a) as anticipated by Batchelor et al. (US 2002/0115559 A1) (of record).

7. With regard to **Claims 1 and 3**, Batchelor discloses a method for producing nitric oxide comprising producing nitric oxide by using a combination of an anionic exchange resin having a nitrite counter ion and a salt (Batchelor, paragraphs 0039-0041, in particular).

8. **Claims 1, 3, 18, 19, 21, 22 and 24** are rejected under 35 U.S.C. 102(b) as anticipated by Smith et al. (XP-002157493) (of record).

9. With regard to **Claims 1 and 3**, Smith discloses a method for producing nitric oxide comprising producing nitric oxide by using a combination of an anionic exchange resin having a diazeniumdiolate-containing composition counter ion and a salt (Smith, Abstract; pages 1148-1150; page 1151, "Synthesis of Polymers of Structure Type 3;" page 1152, in particular).

10. With regard to **Claims 18, 19 and 21**, Smith discloses a method for producing nitric oxide comprising producing nitric oxide by adding phosphate to a nanofiber (polyethylenamine fiber) having a diazeniumdiolate functional group (Smith, Abstract; pages 1148-1149; page 1150, col. 1; page 1151, "Synthesis of Polymers of Structure Type 3" and "Synthesis of Polymers of Structure Type 4;" page 1152, in particular).

11. With regard to **Claims 22 and 24**, Smith discloses a method for producing nitric oxide comprising producing nitric oxide by adding phosphate to a nanoparticle having a diazeniumdiolate functional group (Smith, Abstract; page 1150, col. 1; page 1151, "Synthesis of Polymers of Structure Type 3" and "Synthesis of Polymers of Structure Type 4;" page 1152, in particular).

12. **Claims 1 and 3** are rejected under 35 U.S.C. 102(b) as anticipated by Saavedra et al. (WO 98/13358) (of record).

13. With regard to **Claims 1 and 3**, Saavedra discloses a method for producing nitric oxide comprising producing nitric oxide by using a combination of an anionic exchange resin having a diazeniumdiolate-containing composition counter ion and a salt (Saavedra, Abstract; page 25, line 17 – page 32, line 30; Example 36, in particular).

14. **Claims 1, 3, 6, 7, 11, 12, 18 and 21-24** are rejected under 35 U.S.C. 102(b) as anticipated by Saavedra et al. (WO 96/15797) (of record) (hereinafter, "Saavedra II").

15. With regard to **Claims 1 and 3**, Saavedra II discloses a method for producing nitric oxide comprising producing nitric oxide by using a combination of an anionic exchange resin having a diazeniumdiolate-containing composition counter ion and a salt (Saavedra II, Abstract; page 8, line 3-page 11, line 23; page 17, line 13-page 18, line 4; page 19, line 17-page 21, line 9, in particular).

16. With regard to **Claim 6**, Saavedra II discloses the anionic exchange resin in a gel (Saavedra II, page 17, lines 13-20, in particular).

17. With regard to **Claims 7, 11 and 12**, Saavedra II discloses a method for producing nitric oxide comprising mixing a salt with a gel to produce nitric oxide, wherein the gel has an anionic exchange resin having a diazeniumdiolate-containing composition counter ion therein (Saavedra II, Example IV, in particular).

18. With regard to **Claims 18 and 21**, Saavedra II discloses a method for producing nitric oxide comprising producing nitric oxide by adding phosphate to a nanofiber having a diazeniumdiolate functional group (Saavedra II, Abstract; page 8, line 3-page 11, line 23; page 17, line 13-page 18, line 4; page 19, line 17-page 21, line 9; page 23, lines 10-19, in particular).

19. With regard to **Claims 22-24**, Saavedra II discloses a method for producing nitric oxide comprising producing nitric oxide by adding phosphate to a nanoparticle (polystyrene) having a diazeniumdiolate functional group (Saavedra II, Abstract; page 8, line 3-page 11, line 23; page 17, line 13-page 18, line 4; page 19, line 17-page 21, line 9; page 23, lines 10-19, in particular).

20. **Claims 18, 19, 22 and 23** are rejected under 35 U.S.C. 102(b) as anticipated by Smith et al. (US 5,519,020) (of record).

21. With regard to **Claims 18 and 19**, Smith discloses a method for producing nitric oxide comprising producing nitric oxide by adding a pH adjuster and a salt to a nanofiber (polyethylenimine fiber) having a diazeniumdiolate functional group (Smith, Abstract; Claims 6-10; col. 3-col. 13, in particular).

22. With regard to **Claims 22 and 23**, Smith discloses a method for producing nitric oxide comprising producing nitric oxide by adding a pH adjuster and a salt to a nanoparticle (cellulose) having a diazeniumdiolate functional group (Smith, Abstract; Claims 6-10; col. 3-col. 13, in particular).

Claim Rejections - 35 USC § 103

23. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

24. The factual inquiries set forth in *Graham* v. *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

25. **Claims 8 and 9** are rejected under 35 U.S.C. 103(a) as being unpatentable over Saavedra et al. (WO 96/15797) (hereinafter, "Saavedra II") as applied to **Claim 7** above, and further in view of Fine et al. (US 2003/0064028 A1) (of record).

26. Saavedra II does not disclose the salt being sodium chloride, sodium phosphate, or sodium acetate (**Claim 8**); nor the gel being an ion-free hydrogel (**Claim 9**).

27. With regard to **Claims 8 and 9**, Fine discloses a method for producing nitric oxide comprising the step of mixing a salt (sodium chloride) with a gel (ion-free hydrogel) to produce nitric oxide, wherein the gel has a matrix therein (Fine, paragraphs 0008, 0009, 0017, 0018, 0025, 0038, 0040, 0041, Examples 1 and 2; Claims 1-8 and 16-18, in particular).

28. Thus, it would have been obvious to one of ordinary skill in the art at the time of invention to modify the process of Saavedra II with the salt and hydrogel of Fine in order to obtain a process capable of precisely delivering nitric oxide at therapeutic levels (Fine, paragraphs 0004; 0007-0008, in particular).

29. **Claims 7, 13 and 14** are rejected under 35 U.S.C. 103(a) as being unpatentable over Abrams (US 2,844,546) (of record) in view of Saavedra et al. (WO 96/15797) (hereinafter, "Saavedra II").

30. With regard to **Claims 7, 13 and 14**, Abrams discloses a method for producing nitric oxide comprising producing nitric oxide by using a cationic exchange resin having a hydrogen-atom counter ion (Abrams, col. 7, lines 35-75; col. 8, lines 1-19 and 65-72, in particular). The difference between the process of Abrams and that of **Claim 7** is Abrams does not disclose mixing a salt with a gel to produce nitric oxide, wherein the gel contains the ionic exchange resin therein.

31. With regard to **Claim 7**, Saavedra II discloses a method for producing nitric oxide comprising mixing a salt with a gel to produce nitric oxide, wherein the gel has an ionic exchange resin therein (Saavedra II, Example IV, in particular).

32. Thus, it would have been obvious to one of ordinary skill in the art at the time of invention to modify the process of Abrams with the process of Saavedra II in order to obtain a process capable of producing pharmaceutical compositions that release nitric oxide at therapeutic levels (Saavedra II, Abstract, in particular).

33. **Claim 15** is rejected under 35 U.S.C. 103(a) as being unpatentable over Saavedra et al. (WO 96/15797) (hereinafter, "Saavedra II") as applied to **Claims 7, 11 and 12** above, and further in view of Tucker et al. (US 2005/0036949 A1) (of record).

34. Saavedra does not disclose reacting a hydrogen-atom cation with ascorbate to produce ascorbic acid (**Claim 15**). However, Tucker discloses that ascorbic acid releases nitric oxide for pharmaceutical use (Tucker, Abstract; paragraphs 0010; 0079, in particular). Thus, it would have been obvious to one of ordinary skill in the art at the time of invention to modify the process of Saavedra with the ascorbic acid of Tucker in order to release the nitric oxide.

35. **Claim 16** is rejected under 35 U.S.C. 103(a) as being unpatentable over Saavedra et al. (WO 96/15797) (hereinafter, "Saavedra II") as applied to **Claims 7, 11 and 12** above, and further in view of Benjamin et al. (US 2002/0136750 A1) (of record).

36. Saavedra does not disclose reacting ascorbic acid with nitrite to form nitric oxide (**Claim 16**). However, Benjamin discloses that reacting ascorbic acid with nitrite releases nitric oxide for pharmaceutical use (Benjamin, Abstract; paragraph 0111, in particular). Thus, it would have been obvious to one of ordinary skill in the art at the

time of invention to modify the process of Saavedra with the ascorbic acid/nitrite reaction of Benjamin in order to release the nitric oxide.

37. **Claim 17** is rejected under 35 U.S.C. 103(a) as being unpatentable over Saavedra et al. (WO 96/15797) (hereinafter, "Saavedra II") as applied to **Claims 7, 11 and 12** above, and further in view of Smith et al. (US 5,519,020) (of record).

38. Saavedra does not disclose reacting a hydrogen cation with the diazeniumdiolate-containing composition to produce nitric oxide (**Claim 17**). However, Smith discloses that all that is required to release nitric oxide from a diazeniumdiolate-containing composition is a source of hydrogen cation (Smith, col. 10, lines 62-67, in particular). Thus, it would have been obvious to one of ordinary skill in the art at the time of invention to modify the process of Saavedra with the diazeniumdiolate-containing composition/hydrogen reaction of Smith in order to release the nitric oxide.

39. **Claims 20 and 25** are rejected under 35 U.S.C. 103(a) as being unpatentable over Smith et al. (XP-002157493) as applied to **Claims 18 and 22** above, and further in view of Ignatious et al. (WO 01/54667 A1) (of record).

40. Smith does not disclose the nanofiber being an electrospun nanofiber (**Claim 20**); nor the nanoparticle within or attached to an electrospun nanofiber (**Claim 25**).

41. With regard to **Claims 20 and 25**, Ignatious discloses an electrospun pharmaceutical composition comprising an electrospun fiber of a pharmaceutically acceptable polymeric carrier integrated with a pharmaceutically acceptable active agent

(nanoparticle), wherein the composition achieves maximum bioavailability of a drug moiety (Ignatious, Abstract; Claims 1 and 2, in particular). Thus, it would have been obvious to one of ordinary skill in the art at the time of invention to modify the process of Smith with the electrospun fiber of Ignatious in order to obtain a pharmaceutical composition with maximum bioavailability.

42. **Claims 20 and 25** are rejected under 35 U.S.C. 103(a) as being unpatentable over Saavedra et al. (WO 96/15797) (hereinafter, "Saavedra II") as applied to **Claims 18 and 22** above, and further in view of Ignatious et al. (WO 01/54667 A1).

43. Saavedra does not disclose the nanofiber being an electrospun nanofiber (**Claim 20**); nor the nanoparticle within or attached to an electrospun nanofiber (**Claim 25**).

44. With regard to **Claims 20 and 25**, Ignatious is applied as above. Thus, it would have been obvious to one of ordinary skill in the art at the time of invention to modify the process of Saavedra with the electrospun fiber of Ignatious in order to obtain a pharmaceutical composition with maximum bioavailability.

45. **Claims 20 and 25** are rejected under 35 U.S.C. 103(a) as being unpatentable over Smith et al. (US 5,519,020) as applied to **Claims 18 and 22** above, and further in view of Ignatious et al. (WO 01/54667 A1).

46. Smith does not disclose the nanofiber being an electrospun nanofiber (**Claim 20**); nor the nanoparticle within or attached to an electrospun nanofiber (**Claim 25**).

47. With regard to **Claims 20 and 25**, Ignatious is applied as above. Thus, it would have been obvious to one of ordinary skill in the art at the time of invention to modify the process of Smith with the electrospun fiber of Ignatious in order to obtain a pharmaceutical composition with maximum bioavailability.

Response to Amendment

Applicant's amendments filed November 23, 2010, with regard to the Abstract and Claims have been fully considered and are accepted. The objections to the Abstract and Claims of the previous Office action have been withdrawn.

Response to Arguments

48. Applicant's arguments filed November 23, 2010, with regard to Abrams, Batchelor, Smith, Saavedra, Saavedra II, Smith II, Fine, Tucker, Benjamin and Ignatious (Applicant's Response, 11/23/10, pages 7-14) have been fully considered but they are not persuasive. Applicant's arguments that Abrams, Batchelor, Smith, Saavedra, Saavedra II and Smith II do not teach producing nitric oxide using a salt (Applicant's Response, 11/23/10, pages 7-14) are not convincing. Abrams, Batchelor, Smith, Saavedra, Saavedra II and Smith II do teach producing nitric oxide using a salt, as discussed above. It is noted that many of the cited references use an ionic exchange resin with a buffer, physiological fluids, or in the body. It is well-known in the art that buffers, physiological fluids, and biological fluids contain salts. Further, it is noted that that the "salt" added to amended **Claims 18 and 22** can be the same

component/additive as the pH adjuster. Applicant's arguments that Fine, Tucker, Benjamin and Ignatious do not teach producing nitric oxide using a salt (Applicant's Response, 11/23/10, pages 10-14) are not convincing because Abrams, Batchelor, Smith, Saavedra, Saavedra II and Smith II were used to teach the use of a salt and Fine, Tucker, Benjamin and Ignatious were used as secondary references to teach various other limitations.

49. Applicant's arguments filed November 23, 2010, with regard to Zhang (Applicant's Response, 11/23/10, pages 7 and 11) have been fully considered and are persuasive. The corresponding rejections have been withdrawn.

Conclusion

50. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to BRITTANY M. MARTINEZ whose telephone number is (571) 270-3586. The examiner can normally be reached on Monday-Friday 8:30AM-5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Emily M. Le can be reached on (571) 272-0903. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

BMM
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Examiner, Art Unit 1734

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